

June 13, 2022

Comments on the Draft Toxicological Review of Formaldehyde - Inhalation Toxicity

Submitted online via Regulations.gov to docket EPA-HQ-ORD-2010-0396

These comments are submitted on behalf of the undersigned scientists. We declare collectively that we have no direct or indirect financial or fiduciary interest in the subject of these comments. The co-signers' institutional affiliations are included for identification purposes only and do not imply institutional endorsement or support unless indicated otherwise. We appreciate the opportunity to provide comment on EPA's Integrated Risk Information System (IRIS)'s *"Draft Toxicological Review of Formaldehyde - Inhalation Toxicity"* (Formaldehyde Toxicological Review).¹

Formaldehyde exposure is ubiquitous and occurs in homes, communities, and workplaces. It is a high-volume production chemical with numerous industrial and commercial uses as a solution, disinfectant, preservative or to produce industrial resins used to manufacture adhesives and binders in wood, paper, and other products. It is present in many household products, such as foam insulation, cleaning and personal care products, pressed wood products such as particleboard and plywood, and, as a result, is a common indoor air pollutant found in virtually all homes and buildings.^{2,3,4,5,6,7,8,9,10}

EPA IRIS conducted an assessment for formaldehyde in 1990s, however due to the large amount of new research and data, the Agency re-evaluated the health effects of formaldehyde, releasing an updated draft assessment in June 2010 that was reviewed by the National Academy of Sciences (NAS) in 2011.¹¹ This current draft IRIS document, which is the first EPA assessment of formaldehyde since the 2011 NAS review, was released in April 2022 with a 60-day comment period.

¹ US EPA. (2022). Integrated Risk Information System Toxicological Review of Formaldehyde (Inhalation); Draft. Available: <https://www.regulations.gov/document/EPA-HQ-ORD-2010-0396-0032>

² Agency for Toxic Substances and Disease Registry. Toxicological Profile for Formaldehyde. Atlanta, Georgia: U.S. Department of Health and Human Services, Agency for Toxic Substances and Disease Registry; 1999.

³ U.S. Environmental Protection Agency. Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part F, Supplemental Guidance for Inhalation Risk Assessment). Washington, DC: Office of Superfund Remediation and Technology Innovation; 2009. Contract No.: Contract No.: EPA-540-R-070-002.

⁴ National Toxicology Program. Final report on carcinogens background document for formaldehyde. 2010. Contract No.: 5981.

⁵ Nielsen GD, Larsen ST, Wolkoff P. Recent trend in risk assessment of formaldehyde exposures from indoor air. Archives of Toxicology. 2013;87(1):73-98.

⁶ World Health Organization. Formaldehyde. Geneva, Switzerland: World Health Organization; 2002.

⁷ Plaisance H, Blondel A, Desauziers V, Mocho P. Characteristics of formaldehyde emissions from indoor materials assessed by a method using passive flux sampler measurements. Building and Environment. 2014;73:249-55.

⁸ Salthammer T, Mentese S, Marutzky R. Formaldehyde in the indoor environment. Chemical reviews. 2010;110(4):2536-72.

⁹ Sarigiannis DA, Karakitsios SP, Gotti A, Liakos IL, Katsoyiannis A. Exposure to major volatile organic compounds and carbonyls in European indoor environments and associated health risk. Environment international. 2011;37(4):743-65.

¹⁰ Xiong Y, Krogmann U, Mainelis G, Rodenburg LA, Andrews CJ. Indoor air quality in green buildings: A case-study in a residential high-rise building in the northeastern United States. Journal of environmental science and health Part A, Toxic/hazardous substances & environmental engineering. 2015;50(3):225-42.

¹¹ NAS (2011). Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde. Available: <https://nap.nationalacademies.org/catalog/13142/review-of-the-environmental-protection-agencys-draft-iris-assessment-of-formaldehyde>.

Our comments on the *Formaldehyde Toxicological Review* address the following main issues:

- 1. EPA has not allowed for adequate stakeholder engagement during the comment period.**
- 2. The extent to which EPA has addressed the 2011 NAS recommendations is unclear.**
- 3. EPA did not clearly develop a pre-published protocol.**
- 4. EPA did not model all cancer endpoints.**

We appreciate the opportunity to provide public input. Please do not hesitate to contact us with any questions regarding these comments.

Sincerely,

Swati Rayasam, MSc
Science Associate
Program on Reproductive Health and the Environment
Department of Obstetrics, Gynecology and Reproductive Sciences
University of California, San Francisco

Juleen Lam, PhD, MHS, MS
Assistant Professor
California State University, East Bay

Courtney Cooper, MPH
Science Associate
Program on Reproductive Health and the Environment
Department of Obstetrics, Gynecology and Reproductive Sciences
University of California, San Francisco

Chanese Forté, PhD-PhD, MPH
Assistant Research Scientist
Program on Reproductive Health and the Environment
Department of Obstetrics, Gynecology and Reproductive Sciences
University of California, San Francisco

Nicholas Chartres, PhD
Associate Director
Program on Reproductive Health and the Environment
Department of Obstetrics, Gynecology and Reproductive Sciences
University of California, San Francisco

Tracey Woodruff, PhD, MPH
Professor and Director

Program on Reproductive Health and the Environment
Department of Obstetrics, Gynecology and Reproductive Sciences
University of California, San Francisco

DETAILED COMMENTS

1. EPA has not allowed for adequate stakeholder engagement during the comment period.

Formaldehyde is an environmental justice and affordable housing concern. Lower-income communities are disproportionately at risk of exposure to formaldehyde and resulting health effects from pressed wood products in homes built with less costly building materials. Given this, EPA should have better incorporated into the 60-day comment period opportunities for affected communities as well as academics to engage with EPA on the *Formaldehyde Toxicological Review*. We have stated our concerns about effectively engaging communities in the public comment process in previous comments submitted to EPA.¹²

2. The extent to which EPA has addressed the 2011 NAS recommendations is unclear.

We are generally concerned with whether the 2011 NAS recommendations for the formaldehyde assessment were fully taken into consideration in this assessment.¹³ Given the critical feedback from the NAS, we were surprised to see that the NAS report is rarely mentioned in the draft *Formaldehyde Toxicological Review*. It would be appropriate to more thoroughly outline how changes to the assessment were incorporated to address the concerns raised by this committee of experts.

3. EPA did not clearly develop a pre-published protocol.

EPA, in its Charge Questions to the Peer Review Committee, stated that “The IRIS Program decided to conduct a reassessment of formaldehyde inhalation from scratch on the basis of that review, using transparent and predefined systematic review methods.”¹⁴ We are deeply concerned that we were unable to find an IRIS Assessment Plan or Protocol released in advance of the assessment for peer review comment. Although there were myriad delays of this document, it is troubling that such a protocol may not have been released, which violates the IRIS process for conducting assessments and the stated intent to use “transparent and predefined systematic review methods.” We have commented extensively on the importance of pre-defined protocols, which are foundational to such assessments and play an important role in reducing bias and ensuring transparency.^{15,16}

¹² US EPA. (2022). Science Advisory Committee on Chemicals (SACC); Notice of Public Meeting and Request for Comments on Draft Toxic Substances Control Act (TSCA) Screening Level Approach for Assessing Ambient Air and Water Exposures to Fenceline Communities; Comment submitted by UCSF Program on Reproductive Health and the Environment et al. Available: <https://www.regulations.gov/comment/EPA-HQ-OPPT-2021-0415-0033>

¹³ NAS (2011). Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde. Available: <https://nap.nationalacademies.org/catalog/13142/review-of-the-environmental-protection-agencys-draft-iris-assessment-of-formaldehyde>.

¹⁴ US EPA. (2021). Draft External Peer Review Charge Questions for the IRIS Toxicological Review of Formaldehyde—Inhalation. Available: <https://www.regulations.gov/document/EPA-HQ-ORD-2010-0396-0043>

¹⁵ US EPA. (2021). Comment submitted by UCSF Program on Reproductive Health and the Environment; Availability of the ORD Staff Handbook for Developing IRIS Assessments. Available: <https://www.regulations.gov/comment/EPA-HQ-ORD-2018-0654-0019>

¹⁶ US EPA. (2021). Comment submitted by UCSF Program on Reproductive Health and the Environment: Draft Toxic Substances Control Act (TSCA) systematic review protocol. Available: https://prhe.ucsf.edu/sites/g/files/tkssra341/f/wysiwyg/2022%2002%2018_%20TSCA%20Draft%20Protocol_EPA_UCSF%20PRHE_Comments_FINAL.pdf

4. EPA did not include all cancer endpoints in the estimated inhalation unit risk.

EPA has appropriately determined that the evidence demonstrates that formaldehyde inhalation causes an increased risk of myeloid leukemia in humans. This determination is consistent with previous findings by International Agency for Research on Cancer (IARC)¹⁷ and the National Toxicology Program (NTP)¹⁸, with the NAS affirming the NTP conclusion.¹⁹ EPA, however, does not incorporate the quantitative risk of myeloid leukemia into its estimated inhalation unit risk for formaldehyde, saying that this exclusion is due to uncertainty in the interpretation of the modeling results. It is not appropriate to exclude myeloid leukemia from the quantification of formaldehyde cancer risk, regardless of the uncertainty. EPA's National Air Toxics Assessment (NATA) has identified formaldehyde as the largest nation-wide contributor to cancer risk from air toxics.²⁰ Exclusion of myeloid leukemia from calculation of the IRIS inhalation unit risk will result in consistent underestimation of cancer risk and will adversely affect risk management decisions, particularly in over-burdened communities that experience poor health status in part because of exposure to formaldehyde and other air toxics. EPA should use the results of its best modeling efforts for myeloid leukemia risk from formaldehyde inhalation and incorporate those results into its overall estimate of the inhalation unit risk for formaldehyde. Based on the current draft, that means use of the model results using data from the National Cancer Institute (NCI) study.²¹

¹⁷ IARC. (2012). Chemical agents and related occupations: Volume 100F: A review of human carcinogens. Available: <https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Chemical-Agents-And-Related-Occupations-2012>

¹⁸ NTP. (2021). 15th report on carcinogens. Available: <https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html>

¹⁹ NAS. (2014). Review of the formaldehyde assessment in the National Toxicology Program 12th report on carcinogens. Available: <https://nap.nationalacademies.org/read/18948/chapter/1>

²⁰ NATA. (2014). NATA summary of results. Available: https://www.epa.gov/sites/default/files/2020-07/documents/nata_2014_summary_of_results.pdf

²¹ Beane Freeman, LE; Blair, A; Lubin, JH; Stewart, PA; Hayes, RB; Hoover, RN; Hauptmann, M. (2013). Mortality from solid tumors among workers in formaldehyde industries: an update of the NCI cohort. *Am J Ind Med* 56: 1015-1026. <http://dx.doi.org/10.1002/ajim.22214>